REMARKS

Status of the Claims

Claims 1-4, 6-10, 12, 23-26, 28-29 and 33-37 are pending in the application.

Claims 1, 10, 23, 29 and 33-37 have been amended. While Applicants believe that the originally presented claims are patentable over all of the art cited in the Office Action as well as the other references submitted by Applicants, the claims have nonetheless been amended as follows in order to expedite the application towards allowance. The amendments are therefore made without prejudice or disclaimer, and Applicants reserve the right to pursue the original scope of the claims as provided prior to the amendments, such as through continuation practice. Claims 1, 10, 23, 29 and 33-37 have been amended for clarity and to provide proper antecedent basis. Support for the amendments can be found throughout the published application and more specifically, for example, in paragraphs [0116] - [0118]. No new matter has been added.

In light of the amendments and remarks presented herein, Applicants believe the pending claims are now in condition for allowance, and respectfully request reconsideration and allowance.

The Invention

The current invention is directed to a method of organ augmentation that utilizes two populations of cells with distinct and separate functions, a *first population of cells* that is *encapsulated* and *transiently transfected* to express an *angiogenesis modulating agent*, and a *second population to be assimilated and differentiated* at the target site. Independent claim 1 is directed to a method of organ augmentation using the two populations of cells implanted together in an injectable polymer matrix. Independent claim 23 is directed to a method that involves implanting an encapsulated *first population* of cells and an organ construct that comprises a *second population* of cells at the same target site.

No where in the references cited by the Examiner, either alone or in combination, is there a teaching or suggestion of the claimed invention.

Rejection of Claims 1-4, 6-10, 12, 23-26, 28-29 and 33-37 are rejected under 35 U.S.C. 103(a)

Claims 1-4, 6-10, 12, 23-26, 28-29 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton et al. (US 2003/0007954), in view of Atala et al. (US Patent 6,479,064), MacLaughlin et al. (US Patent 6,692,738), Springer et al. (2000), Rinsch et al. (2001) and Penn et al. (US 2004/0161412 A1, 60/405,274 and 60/424,065). Applicants traverse this rejection.

Naughton et al. (US 2003/0007954)

Naughton et al. teach a three-dimensional stromal tissue implant. In the reference, stromal cells are grown on a biocompatible structure or framework and the implant is used for attachment to various locations. However, Naughton et al. fail to teach *encapsulating* and fail to use two separate populations of cells with distinct functions; 1) *a first population of cells that are encapsulated* and *transfected to transiently express an angiogenesis modulating agent* and 2) a *second population* of cells to be *assimilated* and *differentiated* at a target site.

Furthermore, the secondary references do not remedy the deficiencies in Naughton et al. nor is there any reason to combine the references. Specifically, there is no suggestion that the Naughton et al. reference is unsatisfactory, and there stands no motivation for one of ordinary skill in the art to search for a method of organ augmentation as disclosed in the current invention Moreover, combining Naughton et al. with the other references still does not reconstruct the claimed invention of the current application, that includes *transiently transfecting a first population of cells* to express an angiogenesis modulating agent and *encapsulating the transfected first population of cells* and then combining such encapsulated first population of cells with a *second population* of cells to be assimilated and differentiated at a target site in an injectable polymer matrix as in claim 1 or part of an organ construct as in claim 23.

The deficiencies of the Naughton et al. reference are not overcome by the combination of Naughton et al. with Atala et al., MacLaughlin et al., Springer et al., Rinsch et al. and/or Penn et al.

Atala et al. (US Patent 6,479,064)

Atala et al. describe how to prepare artificial organ constructs from decellularized scaffold whole tissue matrices seeded with endothelial cells to replace organs. Combining Atala et al. with Naughton et al. still does not yield the salient features of independent claims 1 and 23, such as two separate populations of cells, where a *first population* is *transiently transfected* and *encapsulated* and a *second population assimilates* and *differentiates* at a target site.

MacLaughlin et al. (US Patent 6,692,738)

MacLaughlin et al. describe implantable tissue matrices seeded with genetically engineered cells. Combining the teachings of MacLaughlin et al. with Naughton et al. does not yield or suggest the advantage in using two populations of cells such as those cited in independent claims 1 and 23 of the claimed invention, where a *first population* is *transiently transfected* and *encapsulated* and a *second population assimilates* and *differentiates* at a target site.

Springer et al. (2000) and Rinsch et al. (2001)

The Springer et al. and Rinsch et al. references are understood to have been cited by the Examiner to overcome the lack of encapsulation by the Naughton et al. reference. Springer et al. teach capsules containing VEGF expressing myoblasts and Rinsch et al. teach encapsulation of genetically engineered myoblasts to express VEGF or FGF-2. However, combination of the two references with Naughton et al. still fails to teach or suggest the use of two separate populations of cells, where a *first population* is *transiently transfected* and *encapsulated* and a *second population assimilates* and *differentiates* at a target site.

More importantly, Rinsch et al. teach away from the use of VEGF encapsulated cells. On page 3 of the Office Action, the Examiner cites page 526, col. 2 as evidence of blood vessel formation in and around the implant, however only animals receiving FGF-2 were analyzed by microangiography and their results reported as evidence. Rinsch et al. found that "animals receiving $VEGF_{121}$ or $VEGF_{165}$ had no significant improvement in flap survival over controls." (See Rinsch et al. page 525, col. 2.) Moreover, Rinsch et al. go even further by stating "[t]he

failure of VEGF in this model" (page 529, col. 1). Thus, Rinsch et al. suggest encapsulating VEGF-producing cells is not effective in promoting vascularization possibly due to the low doses of VEGF administered (page 529, col.2).

Penn et al. (US 2004/0161412 A1, 60/405,274 and 60/424,065)

Penn et al. also do not remedy the deficiencies of Naughton et al. Penn et al. disclose stimulating transplanted cells to express VEGF. However, Penn et al. do not teach or suggest co-implanting two separate cell populations with distinct functions. Thus the combination of Penn et al. with Naughton et al. does not teach or suggest the use of two separate populations of cells, where a *first population* is *transiently transfected* and *encapsulated* and a *second population assimilates* and *differentiates* at a target site.

Thus none of the cited references, alone or in combination, teach or suggest the invention as a whole, much less the use of two separate populations of cells, where a *first population* is *transiently transfected* and *encapsulated* and a *second population assimilates* and *differentiates* at a target site.

CONCLUSION

In view of the above remarks, Applicants' respectfully request reconsideration and allowance of the application. The Examiner is invited to call the undersigned at (617) 439-2948 if there are any questions.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 141449, under Order No. 105447-0002.

Respectfully submitted,

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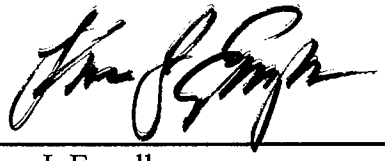

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